A Perspective on the War on Cancer

Vincent T. DeVita, Jr., MD, *New Haven, Connecticut*

On December 23rd, 1971, President Richard M. Nixon signed the National Cancer Act that was to launch the nation's "War on Cancer." The mandate as stated in the Act itself was "to support basic research and the applications of the results of basic research, to reduce the incidence, mortality and morbidity from cancer." There were many specific suggestions in the language of the Act to achieve these goals, which were often couched in the term "insofar as feasible" in recognition of the limitations of the tools available at the time.

The Cancer Act was the brainchild of Mary Lasker, a New York philanthropist renowned for her insight on public health issues. She already had to her credit as an activist the recognition of streptomycin as the first useful drug for tuberculosis and the national high blood pressure program, which was to lead in the reduction of fatal strokes in the United States. She was also the driving force behind the establishment of the disease-oriented institutes at the National Institutes of Health, maintaining (quite correctly) that the public would support research on diseases they recognized, not the research components they didn't. And, up to 1971, Mary Lasker had helped found the National Cancer Institute and the National Heart Institute. She was the major force behind the American Cancer Society's decision to support basic research with some of its funds. Thus, she was no neophyte in amassing support for major public health issues.

In reference to the Cancer War, in 1970 the recently reported cures of some cancers with chemotherapy had convinced Mary Lasker that the missing piece to the therapeutic puzzle—effective systemic therapy—had been found. She believed we had reached a "critical mass" of tools available to launch the War on Cancer. To emphasize this point, a year after the Act was signed, the Prize jury of the Lasker Foundation awarded the prestigious Lasker Prize in Medical Research to multiple investigators who were involved in the experiments that showed that some types of advanced human cancers were curable by drugs. The studies that led to the prizes addressed the generic question of the curability of any cancer by chemotherapy and were the noblest therapeutic experiments of the 1960s in the cancer field.

Mary Lasker marshaled vast amounts of public support for the passage of the 1971 National Cancer Act, including an open letter to the public by the late Ann Landers, a close personal friend, which pressured Congress into action. The problem was that Mary Lasker was a lifelong Democrat, and the initial effort to sponsor the Act was by another Democrat, Senator Ted Kennedy. A combination of Lasker and Kennedy was not likely to get President Nixon's sympathetic support. The politics of how Mary Lasker's vast political network transformed the Cancer Act into something Nixon would support is beyond the scope of this brief piece, but makes interesting reading.

A special commission led by then Texas Senator Ralph Yarborough shaped the essence of the Act. The commission members themselves were, for the most part, hand-picked by Mary Lasker. They were well known lay and medical advocates for an expanded national effort to attack the cancer problem.

To motivate everyone, there was the implication by Mrs. Lasker, and those intimates around her, that with a concerted effort, the diseases known as cancer could be conquered by the nation's bicentennial, a mere five years away. Considering that, in 1971, cancer was the most feared disease in the minds of the average American, this was an easy sell—but was one aspect of the War on Cancer that no physician or scientist ever thought was achievable. The press, however, were not to forget it. This hype, and the use of public opinion to go over the heads of the scientific establishment to Congress, incurred the wrath of most of NIH and academia. In the debate that followed the introduction of the Act, even the American Medical Association was against its passage.

The two main arguments against it were that 1) money couldn't buy ideas and 2) research was a process that was best left unfocused. Targeting research at cancer, it was widely said, would be a subversion of the fundamental process of research and drain resources from other important areas. There was another even more vexing issue. The mandate of the Act, cited above, required the development of programs for the application of the results of research, heretofore considered out of

From the Yale University School of Medicine, New Haven, Connecticut.

Received on August 23, 2002; accepted for publication August 28, 2002.

No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this article.

Reprint requests: Vincent T. DeVita, Jr., MD, Yale School of Medicine, 333 Cedar Street, New Haven, CT 06520.

the realm of an institution like NIH, exclusively devoted to seeking scientific truths. Mary Lasker also had a deep-seated distrust of the NIH bureaucracy and, at her insistence, some programs devoted to research applications mandated by the Act were written in as budget line items to discourage their assimilation into standard NIH programs.

A controversial part of the Act also gave the National Cancer Institute a degree of autonomy at NIH. The NCI Director and its National Cancer Advisory Board were to become Presidential appointments, and, at least in the early years, special budgetary authority allowed NCI to bypass both the Public Health Service and the Office of Management and Budget and go directly to the President on budgetary and other matters. The NCI Director also reported to the newly created, presidentially appointed President's Cancer Panel, which oversaw the National Cancer Program, which was meant to extend in its entirety beyond the confines of the NIH. This panel was composed of a lay Chair, a basic scientist, and a clinician. Its function was management oversight, and it reported directly to the President. In the early years, the panel met monthly and monitored all aspects of the program quite closely and effectively.

The War on Cancer became a popular target in the press. This label was an unfortunate term to use at the time, with the Vietnam War raging and controversial, and body counts an every day event. The press was to demand a similar accounting for the War on Cancer from the NCI, represented by the pace of reductions in cancer deaths. To move rapidly to meet the ambitious timetable, NCI also used the research contract mechanism to support new research projects. Contracts were then and are now the anathema of research at NIH, which further fueled the controversy. Closely watched by many skeptics, by 1974, headlines in the newspapers in the Washington area were already implying mismanagement of NCI contract programs and lack of results, e.g. a reduction in mortality rates.

THE IMPACT OF THE CANCER WAR

But the Cancer Act worked. It turned out money *did* buy ideas. Putting brilliant people to work on a problem broad enough to give wide range to their imaginations generated ideas aplenty. Paying attention to both research and the applications of the results of research turned out to be quite possible and beneficial to NIH, in general, and certainly to the public at large. Most NIH institutions have now adopted this approach. Only the timing was off: it wasn't until almost 20 years later, in 1990, that both overall incidence and mortality from cancer in the U.S. began to fall. There were, however, clear signs this was coming a decade and a half earlier, for those who wanted to see them. Age-specific and disease-specific mortality rates began to decline dramatically, first at the youngest end and then creeping upward until the overall effects were noted in 1990. The decline in mortality has continued since 1990, and it deepens every succeeding year.

What happened? In simple terms, the resources provided by the Cancer Act flowed in two general waves. About 80%–85% of funds in the first wave went to support basic research, depending on how you classified it, and the training of young scientists. Another 15%–20% went into the second wave to the support of applications programs, such as improvements in chemotherapy and radiotherapy and the training of specialists, including those who gave birth to the new field of medical oncology. A major beneficiary of the second wave was the NCI's Clinical Trials program, which was increased in funding tenfold in less than a decade. This led to the widespread technical improvement of—and access to—the tools of cancer diagnosis and treatment, simultaneously applied rather than in sequences determined by conventions of the day. A striking result of this expansion and the growth of combined modality treatment programs, often overlooked, is the marked reduction in morbidity from treatment for the majority of cancers—one of the Cancer Act's original mandates.

There are many examples to choose from, but the management of breast cancer is one particularly good example. In 1971, when a breast lump was found, a patient had a biopsy under general anesthesia. Seventy-five percent of lumps were expected to be benign, and patients expected to beat the odds. If, however, at the time of surgery a frozen section examination found it malignant, the treatment of choice was radical mastectomy; it was done under the same anesthesia, and the patient awoke to the shock of a denuded chest wall. The practice at the time was for radiation to be used afterward—and the complications of adding radiation therapy to a chest wall scraped clean by a radical mastectomy were severe and disfiguring. Adjuvant chemotherapy was just an idea at the time, and no further treatment was generally offered to these patients. This was too much treatment for small lesions, but not enough for large ones. Mortality was not really affected by these approaches, and the morbidity was horrendous. Now, after needle biopsy and a discussion of all options with the patient, in most cases the breast is salvaged by lumpectomy, with radiation therapy used instead of radical surgery and effective adjuvant chemotherapy therapy follows. The cosmetic effect is excellent, morbidity is much less, survival has improved dramatically, and national mortality from breast cancer has declined—a combined effect of earlier diagnosis and better-integrated treatment. This transformation is the result of expanded, properly designed clinical trials testing new approaches and good ideas. There are many other

examples like this; every sub specialty has them, including the example of colorectal cancer, another common tumor. Colon cancer mortality has decreased by 40% over the past three decades, due both to early diagnosis and effective adjuvant treatment. The improvement in surgical techniques has also significantly reduced morbidity.

One problem with the interpretation of these changes is that the 30-year time span since the passage of the Cancer Act has distorted our focus. Not too many of our current professionals have lived through all the changes. Therefore, there aren't many who can put them into proper perspective. And to each cancer patient today, diagnosis and treatment is still a very difficult experience—but they cannot really appreciate how much more difficult it was in 1971.

The first infusion of massive funds into basic research programs began in reality in 1972. As any investigator knows, it takes several years to get laboratories running at full speed. So the critics of 1974 were correct in their interpretation of the lack of tangible benefits, although the rush of new money to established laboratories, much of it in the form of research contracts, fostered some major discoveries even in those early years.

The confusion over the use of research contracts to accelerate the program was a major problem because the use of contracts was regarded as the essence of targeting. The prevailing opinion was that only peer-reviewed grants could support good science. Even good research supported by contracts was criticized. Again, there are many cases where this occurred, but the work on cancer viruses serves as a good example. The Special Virus Cancer Program initially used the research contract as its support vehicle and was the most criticized special initiative of the National Cancer Program. Yet it spawned the field of molecular biology. For example, at a time early in the growth of the field of molecular biology, when the NCI budget was 23% of the NIH budget, the NCI supported 50% of all NIH research in molecular biology, a great deal of it in cancer virus research. Out of this came the knowledge of reverse transcriptase, oncogenes, suppressor oncogenes, and numerous elements of the systems cells use to talk to one another, the essence of the malignant process. All of them are today's targets of prevention, diagnosis, and therapy. The contract-supported Special Virus Program investigators ultimately garnered a significant number of Nobel Prizes. In addition the supply of the enzyme, reverse transcriptase from a research contract studying avian myeloblastosis viruses jump-started the biotechnology industry.

When the AIDS epidemic hit the nation, it was the National Cancer Program that first responded because it supported the nation's only research program on retroviruses. The first AIDS drugs came from NCI's cancer drug development program. The War on Cancer ultimately served as a model for vital components of the national AIDS efforts. In addition to becoming a premier research facility for the new field of molecular biology, the Fort Dietrich Maryland Army base, which had been given to the NCI to "turn swords into plowshares" by that act of Congress, also provided 500 liters of HIV-infected cells that made possible the first reliable diagnostic test for AIDS, which has saved many lives.

Cancer drug development, initially almost exclusively the province of the NCI and some university investigators, has become a thriving industry around the world. It made effective treatments available to thousands of cancer patients previously without treatment options, thanks to NCI's most controversial contract supported program, the Cancer Chemotherapy National Service Center.

In other words, basic science and the application of the results of basic science both flourished, and, as the late Benno Schmidt, Sr., the first Chair of the newly established President's Cancer Panel, was fond of pointing out to Cancer Act critics, "a rising tide floats all boats." The NIH budget for its other institutes increased faster after the Act was passed than before, although not as rapidly as NCI's budget. This belied the argument that focusing on one disease would starve the research efforts into others. And, it has continued that way.

Yet Mary Lasker was wrong in 1971. We had not achieved critical mass at that time. This accounted for the long time frame for the positive results of the program to evolve. What the Cancer Act has done is to provide the resources that have now created what I like to refer to as a "critical mass of *usable* knowledge." The reduction of mortality we are now witnessing is actually not due to the creation of this usable knowledge in molecular medicine but is primarily due to the improvement, access, and distribution of older technology supported by the cancer program. We are just beginning to experience the effects of the "critical mass of usable knowledge" in the clinic. In a sense, the two waves are now washing up on shore together. This means that, if we can maintain our momentum, the best is yet to come. It's interesting today, as we hear of one major discovery after another in all of biomedical research on a daily basis, to think about how often current work is derived from the special initiative that was the War on Cancer. AIDS was just one example of how the advances spilled over to other fields; there are many others.

THE CANCER ACT IN THE NEW MILLENIUM

It would be nice to be able to say that the true impact of the National Cancer Act is now widely appreciated. It is not. Surely, many of the critics are no longer vocal, but the legacy created by the way the cancer program

was started still lingers. Also, with time, the special features of the Cancer Act—particularly those in regard to the governance of science at the NCI—have been allowed, even encouraged, to erode. In addition, although the NCI developed very effective applications programs, its initial authorities did not extend to programs that were responsible for the access to and delivery of health care. Thus the full promise of the original Cancer Act could not be reached despite the fact that over 40 billion dollars of public money have been expended on cancer research.

There have been marked changes in the landscape of the research environment since 1971. One of these changes is the birth of cancer-related advocacy groups. Absent in the early years of the Cancer Program, they are abundant now. While their impact is largely beneficial, the tendency for disease-oriented groups to advocate for a single type of cancer at a time is often alarming to administrators of large research programs. Many of what we would consider as major advances related to one cancer or another came from unexpected sources not classifiable as research related to those diseases.

The other major change in the landscape is that the NCI is no longer alone in its leadership of cancer research or the applications of the results of research. The effort has broadened to include major programs in the private sector, other government agencies like the Center for Disease Control, Health Resources and Services Administration, and the Defense Department. And if the goal is to broaden the reach of the Cancer Program, it needs to include the funding agencies for health care.

About three years ago, in order to try to bring some order out of the chaos of the large number of competing groups and organizations, former President George Bush and Mrs. Bush decided to cosponsor a new organization called the National Dialogue on Cancer (NDC). Its mission was just what the name implied: to open and maintain a dialogue among all organizations and advocacy groups involved in the cancer effort, to clarify positions such that common goals can be set and achieved. In other words, the mission was to address a part of the national War on Cancer that was not achievable by the Cancer Act of 1971. The NDC now has over a hundred collaborating partners. The operational cochairs of the NDC are Senator Dianne Feinstein and Dr. LaSalle Leffall, a noted cancer surgeon. The financial support for the development of the NDC initially came from the American Cancer Society.

THE CANCER ACT OF 2002

After a few meetings of the NDC, with vigorous debate about the status of the original Cancer Act and its successes and failures, Senator Feinstein became interested in the possibility of a new Cancer Act, one that would focus new resources on the issue of cancer control in a more global way while maintaining the momentum for the support for basic research. To accomplish this, she asked this author and Dr. John Seffrin, the CEO of the National American Cancer Society, to select and cochair a new committee, completely separate from the NDC, that came to be known as the National Cancer Legislative Advisory Committee (NCLAC). The committee of twenty-two members, made up of clinicians, basic scientists, and leaders of organizations representing researchers and patients alike, was given the task of shaping the contents of such a new program. After 18 months of work, over 300 interviews, hearings that took testimony from all major agencies and their components, and eight round table workshops, the committee produced its report in September of 2001. As a result, earlier this year, Senator Feinstein and twenty-nine cosponsors submitted a bill for the consideration of the senate dubbed the The National Cancer Act of 2002. In April 2002, a similar bill was submitted to the House of Representatives with eleven cosponsors.

The NCLAC experience was interesting. The same anxiety aroused by the original act turned out to be very close to the surface, and it soon became apparent the work of NCLAC would be almost as controversial. The first major issue was the fear that, with only twenty-two members, some important group would be underrepresented. The second fear was that by focusing on the deficiencies in cancer control, the NCLAC report would lead to the diversion of funds from basic research. Most controversial of all was any attempt by NCLAC to re-examine the structure of the National Cancer Program with an eye towards suggesting a new organization. In truth, representation at NCLAC, especially through the interview process, was broad; the report, as others had before it, strongly endorsed the continued path of doubling the NCI and NIH budgets and then adding on the funds required for some special programs focusing on access to care.

Other recommendations included suggestions for the coverage of all patients with cancer by Medicare, regardless of age, to alleviate problems related to access to care. In addition, an expansion and funding of the CDC program to develop state cancer control programs in all the states was recommended including a recommendation to mandate a link between state cancer control programs and the NCI's Cancer Centers, in addition to state health departments. This would provide a powerful nationwide network with the hub being the crucibles of research represented by the NCI Comprehensive Cancer Centers. To meet the expanded CDC program, the NCLAC committee felt it would be necessary for the NCI to examine the structure and support for its current cancer center programs. Equal geographic distribution of cancer centers couldn't be achieved in 1971 due to

the limited research base in the country at that time. In addition, thirty years of experience with NCI centers has taught us that the current support instruments for NCI cancer centers, the Cancer Center Support Grants, have become creaky, inflexible, and outdated. Yet we are at a time when cancer centers, as intended in the original mandate, should be able to assure all cancer patients, not just access to state-of-the-art care, but access to new advances as they roll off the assembly line.

In the debate over the proper governance of the national effort against cancer, "If it ain't broke, don't fix it!" was the rallying cry we heard most of all. But, indeed, testimony of program leader after program leader made it apparent that the governance structure developed in 1971 was "broke" largely due to the changing landscape created by the very success of the National Cancer Program. With NCI once again focusing increasingly on fundamental research, and many applications and access programs in other public and private institutions, the most popular suggestion to the NCLAC committee was for some oversight of the National Cancer Program by an individual, or group, situated in the executive branch, on a full time basis. The role of this person, or group, would be to see that components of any new act, especially budgetary review, would each receive adequate attention regardless of what sector was to be responsible for them. In the final report, due to the controversy, these specifics were much subdued in favor of a recommendation that some other body, beside NCLAC, examine ways of establishing a mechanism of accountability for the new cancer programs of 2002.

The current bills in Congress incorporate some, but not all, of the NCLAC suggestions and are an excellent start to finishing what was begun in 1971. Given the current favorable trends in national statistics and the power of the new discoveries, with a concerted effort to use and improve the structure provided by the original Cancer Act, cancer, still the most feared disease in the minds of the American public, will become a far less threatening killer within the next two decades. The momentum created by the original Cancer Act has virtually assured this will happen. The only question remaining is when, and the when will be determined by the will we have as a nation in finishing the job a small group of prescient people started three decades ago.